Experimenta lucifera

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The Professor, The Institute and DNA. By R. J. Dubos. Pp. 238. (Rockefeller University: New York, 1976.) $14.50.

IN the late 1930s, during my early days at Columbia University, I had frequent occasion to visit the Rockefeller Institute for Medical Research, as it was then called. The uninviting structures on Avenue A near the East River were not easy of approach. True to its character of a citadel of learning, the door of the Institute was fortified by gruffness; and after passing inspection by Cerberus or Cerbera, the visitor had to be accompanied to his destination by a special young man. In my case this destination usually was the laboratory of the organic chemist Max Bergmann, much admired by me. I had known Bergmann when he directed a Kaiser Wilhelm Institute in Dresden; here in New York he shared the uneasy fate of his generation of German emigrants. On seeing me, he would exclaim: "*Zuerst rauchen wir eine Friedenspfeife!*" producing a large glass jar in which a package of cigarettes was kept in a controlled habitat. Occasionally, he conducted me afterwards to another laboratory, that of P. A. Levene or D. D. van Slyke; and sometimes I would come upon the light-brown shadow of an elderly mouse-like figure tripping along the corridor walls. This, I was told, was Dr Avery, a name not unknown to me as that of the greatest expert on the pneumococcus, although at that time I could not have known how important his name would become to me a few years later.

These reminiscences were brought on by an uncommon book about an unusual man, Oswald T. Avery (1877–1955). It is, in my opinion, a very good book, and I enjoyed reading it. As the title indicates, this is not merely a scientific biography. The book operates on several intercommunicating levels, taking into account the man, the time, and the place; and painting, with extraordinary competence, the ever-changing human and scientific backdrops. This competence is not entirely surprising: René Dubos, apart from being a very good writer, was a member of Avery's department from 1927 to 1941, and the warmth of personal contact and observation is felt throughout the narrative.

Born to English parents in Halifax, Nova Scotia, Avery was taken to New York City at the age of ten, when his father, who was a Baptist clergyman, was invited to be pastor of the Mariners' Temple on the lower Eastside, even at that time a pretty horrible part of the city. But five years later, the father was dead, and the three sons were brought up by the mother who must have been an energetic lady. Oswald Avery, aside from becoming an accomplished cornetist, got a good education: first something called, soberly, the New York Male Grammar School, then Colgate Academy, Colgate University, and finally, between 1900 and 1904, the College of Physicians and Surgeons of Columbia University, which was then one of the best finishing schools for clinicians. The latter seems to have finished him in more than one sense: in went a lively, communicative young man, majoring in the humanities, excelling in oratorical contests, playing the cornet, leading the Colgate University band, and clearly not particularly attracted to the natural sciences; out came what I would term, perhaps with some exaggeration, a scientific recluse. This shock of confrontation is not a very rare event: I have noticed it often in several generations of medical students, when I taught at the same medical school; only few of those affected, I am sure, turned into other Averys; mostly they became psychiatrists or even psychoanalysts.

Scientists in general lead uneventful lives, with the exception of the few who, for instance, are guillotined during the French Revolution or killed by highway robbers in Southern France. What counts is their inner history to which their published papers afford only precarious access, for the history of ideas, and especially of scientific ideas, is a slippery discipline. But in the present instance, Dubos has succeeded in producing as multidimensional an image as is possible.

With the exception of a very short period, after graduation, in medical practice, Avery devoted his entire life to research in bacteriology and immunology, first in a now extinct private institution, the Hoagland Laboratory in Brooklyn, and since 1913 in the Rockefeller Institute, where he remained until he was 71. The last few years of his life were spent, let us hope serenely, in the South. Or as Dubos puts it: "In 1948, he decided that he had shot his bolt; as he no longer felt able to function effectively in the scientific arena, he retired to Nashville, Tennessee". Each of the verbs in the preceding sentence could lend itself to a philosophical analysis which I shall not attempt here, except to wonder why society seems to reserve circus acrobatics and science for the very young, assuming that these occupations require muscular vigour rather than wisdom. Why had, for instance, Telemann not yet "'shot his bolt,'" when at the age of 81 he wrote what is widely considered as his greatest work, the oratorio *Der Tag des Gerichts*? The multiplicity of possible answers shows that we have not yet found the corect one.

The major part of the book is devoted to a detailed and lucid discussion of the problems investigated by Avery during his 35 years at the Rockefeller Institute. This is done in five chapters the titles of which will indicate the areas under study: 'The Lure of Antiblastic Immunity and the Chemistry of the Host'; 'The Chemical Basis of Biological Specificity'; 'The Complexities of Virulence'; 'Bacterial Variability'; and 'Heredity and DNA.' It will be recognised that Avery was one of the early microbiologists who understood the dominating role that chemistry was to play in biology. This was, incidentally, quite in harmony with the *genius loci* of the Rockefeller Institute, which in this respect, as in many others, was a most remarkable place. Dubos does full justice also to this side of his story; and the Institute, with its members, seminars, conferences, and, especially, its memorable capitalistico-monastic lunch room, is one of the indispensable elements of his account.

Avery was comparatively late in starting, but he lasted: his most important work was published when he was past sixty-six. The pneumococcus was his microcosm; he showed that general principles of great import can be derived from little things if it is given to the researcher to join penetration to perseverance, and bold deduction to honest induction. As always, what counts is the balance, the mixture; but has anybody in science succeeded in mixing himself, in filling his own recipe?

Avery became interested in the pneumococcus because one of the principal projects studied at the Rockefeller Hospital was the development of a serum therapy for lobar pneumonia. I do not believe the practical results of his research ought to be stressed, but out of this work there emerged a new understanding of the chemical basis of antigenicity, and, even more suprisingly, the recognition that genes were made of DNA. These glories may be taken to demonstrate the stupidity of our era of target-directed research. Actually, science has never operated entirely without goals; but the goals were chosen by a few reasonable men, not by frightened politicians or bureaucrats, and were enforced with

Avery's Department, 1932.
Seated (left to right): T. Francis, Jr, Avery, W. F. Goebel
Standing: E. E. Terrell, K. Goodner, Dubos, F. H. Babers

tact and imagination. The directors of the Institute and the Hospital were wise enough to leave such a man as Avery in peace. They had trust in him; something that no 'peer group' with its silly priorities can afford or accomplish. The absence of frenzy is one of the main impressions I get from Dubos' description of Avery's laboratory.

The existence of many immunologically different pneumococcus types had been known for some time. In 1916, Avery's intimate friend, Alphonse Dochez—I knew him very well during his years as a Columbia professor—discovered that type-specific soluble material was released into the culture fluids by the organisms. These observations, extended and refined in the course of several years, finally led to Avery's collaboration with Michael Heidelberger, and later also with Walther Goebel, and to the identification of a host of type-specific bacterial polysaccharides as the basis of the immunological specificity of the various strains. It is not too much to say that this work had a profound influence on the growth of immunochemistry and on later concepts of "the chemical aspects of biological specificity." This was the title of the series of Jesup lectures that I gave at Columbia University four years after Avery's death. His name was mentioned more often than anybody else's, with the exception, of course, of my own.

Leaving aside a large number of interesting and important investigations by Avery and his collaborators—almost all within the confines of his 'pneumocosm'—I should like to move rapidly to what most of us will consider the most illuminating, the *luciferrimum*, of his many *experimenta lucifera*. (Dubos quotes Francis Bacon's distinction, in his *Instauratio Magna*, between "experiments of light" and "experiments of fruit.") I refer, of course, to the work on the biological activity of DNA. In view of the witches' brew now being stirred all over the world, with "recombinant DNA" as its main ingredient, I can only hope that the title of this essay will not have to be changed to *experimenta Luciferi;* although the Devil hardly needs experiments to make his point.

Less than sixteen years—1928 to 1944—were required for the first fundamental observation to lead to the definite proof that DNA was the instrument of genetic specificity. That it actually took much more time before this proof was accepted generally, was due to obtuseness, malevolence, and the desire to protect various vested interests. I remember the names of both the heroes and the villains in this story, but only a few of the first will be mentioned here. When the transformation of pneumococcal types *in vivo* was discovered in 1928 by F. Griffith, there were no loud objections, perhaps owing to the rapid confirmation of his findings in other laboratories or because most bacteriologists at that time were Lamarckians. But for some reason the observations were filed away and, had it not been for Avery, they might have slumbered a long time. It was in Avery's laboratory that Dawson and Sia achieved transformation in *vitro* and that Alloway described the isolation of a crude transforming factor. All this was accomplished before 1933; and Dubos takes great pains to explain why more than ten years elapsed before the next, and in every respect final, publication. Such explanations are really not necessary: before World War II, science was not yet an achievement sport; speed records formed no part of the accomplishments of a scientist as they do now. Griffith and Avery are both quoted as deprecating hurry; and Dubos tells us that Avery liked to recall "the words of an old black patient who watched, with amused surprise, the young doctors rushing about the wards of The Johns Hopkins Hospital: 'What's your hurry, Doc? By rushing that way, you passes by much more than you catches up with!'".

When in 1944 the epochal paper by Avery together with Colin M. MacLeod and Maclyn McCarty appeared, it certainly was something worth waiting for. The stages leading up to this publication and the all-in-all shabby reception granted it by the experts are well documented in the book, although more could, and probably will, be said eventually. As to the effect that the identification of the transforming principle as a form of DNA had on me and on the direction of my subsequent work, I have described it before. Avery himself obviously realised the implications of his discovery much more profoundly than he was willing to put into print. The letter he wrote to his brother Roy on 26 May, 1943, is particularly instructive in this respect. His entire character as a scientist—relentless perseverance, courageous imagination, extreme caution—can be developed from this document.

Many readers will, I am sure, find one chapter especially moving—namely, chapter twelve, entitled "As I Remember Him." I have never seen this done before in the biography of a scientist. To the limited extent that a scientific investigator is also a human being, the carving of the private bust calls for an unusually tactful and sensitive observer; and this René Dubos must have been in the many years he spent with or near Avery. Nevertheless, Avery was an extremely private person, and there must have been a wall around him, not of his own building—a wall that constrained him as it restrained access to him. I am not sure that we can ever understand another man so as to resurrect him on paper. The reason why figures invented by great novelists strike us as so alive is that they are invented. At any rate, what I got out of reading about this shy, puritanical, disciplined, and cautious man was a renewed awareness of the poverty of greatness.

As I said at the beginning, this is an interesting book. It is also very well produced, with 22 illustrations, some quite fascinating, and with a good index. It should be read by all who consider themselves part of the 'biomedical community', and molecular biologists should read it twice. Even philosophers and historians of science, if they can spare a few moments from their contemplation of the dark side of the Reverend Moon, will find the book profitable. □

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